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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,809	07/30/2001	Robert David Possee	46309-257438	7430

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EXAMINER	
MARVICH, MARIA	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 01/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,809	POSSEE ET AL.	
	Examiner	Art Unit	
	Maria B. Marvich, PhD	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/23/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment and request for continued examination filed 10/21/05 and Declaration under 35 USC 1.132 originally filed 10/21/05 and resubmitted 12/7/05. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/21/05 has been entered. Claims 1-26 and 35-50 have been canceled. Claims 27 and 29-34 have been amended. Claims 27-34 are pending in this application.

Response to Amendment

The Declaration under 37 CFR 1.132 filed 10/21/05 is sufficient to overcome the rejection of claims 27-34 based upon Clark et al in view of Patel et al and Kitts et al in view of Patel et al. Any rejection of record in the previous action not addressed in this office action is withdrawn.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent

Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Specifically, figures 2 contain sequences that are not identified by sequence identifier numbers. If the sequences can be found in the sequence listing it would be remedial to insert the appropriate SEQ ID NO:s. If not, a new sequence listing, CRF and letter stating that the contents of the sequence listing and the CRF are the same and contain no new matter are required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for cloning a gene comprising providing a naked circular replication –deficient baculovirus vector, does not reasonably provide enablement for a method for cloning a gene comprising providing a naked circular replication –deficient baculovirus vector that lacks *p35*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. **This is a new rejection.**

1) Nature of invention. The instant claims are drawn to a method for cloning a gene comprising providing a naked circular replication–deficient baculovirus vector and providing a rescue vector comprising the gene to be cloned and a nucleic acid capable of restoring the replication of the replication deficient baculovirus and allowing the vectors to recombine in an insect cell.

2) Scope of the invention. Specifically, claims 29-32 recite that the replication deficient baculovirus lacks a functional *lef1-12, dnapol, pl43, p35, ie-1, p47, ORF1629* or *pp31* gene which function is restored by the rescue vector.

3) Number of working examples and guidance. Applicants exemplify the recited method by generation of a replication defective baculovirus genome, ACMNPV, deleted of 1) full-length *lef-2,* 2) full-length *ORF1629, lef-1* and protein kinase 1 or 3) a small part of *ORF1629*. In the recombination reactions, a rescue vector was used comprising respectively 1) *lef-2* (pUC8/6/8 described on page 20, last paragraph), 2) regions overlapping *lef-2, ORF1629, lef-1* and protein kinase 1 (pAcBglII-C, second paragraph, page 27) and 3) a vector described only as comprising a lacZ coding region (page 29). Following recombination in an insect cell, recombinant baculovirus comprising the transgene were generated.

4) State of the art. Baculovirus is a eukaryotic virus that has been exploited to function as an expression system for transgenes as baculovirus is believed to have potential in therapeutic applications. Clark et al teach methods of generating recombinant baculovirus without utilizing cloning steps (see e.g. column 5, line 1-7). As shown in figure two, the method involves the co-transfection of a replication deficient baculovirus deleted of *p35,* an apoptosis repressor gene, that has been linearized by restriction within orf-1629, and a "rescue" vector comprised of baculovirus *p35* and *orf-1629* genes as well as the transgene. Other methods of generation of baculovirus involve maintenance of baculovirus in bacteria in which foreign genes are inserted by transposition. Disadvantages of previous methods are said to be the laborious nature of the methods due to the large nature of the vector (130 kb) and the multiple manipulations required to

identify recombinants. As well, contamination of parental vectors is a constant problem in methods of preparation.

5) Unpredictability of the art. In the amendment and Declaration filed 10/21/05, applicants have argued that the vector of Clark et al is only suitable for use in apoptosis deficient host cells such as *T. ni*. Specifically, applicants argue that the vector cannot be grown in intermediate hosts other than the apoptosis deficient insect cells (see page 3 of the Declaration filed 10/21/05. Hence by applicants' own admission, the method is not enabled for use with *p35* as the method requires that the vector be capable of being maintained in bacteria.

6) Amount of Experimentation Required. The invention recites use of a baculovirus that is replication deficient due to a lack of functional gene selected from a broad group of genes. Given that applicants have argued that providing a naked circular replication –deficient baculovirus vector that lacks *p35* does not reasonably provide enablement for a method for cloning a gene, the instant invention would require undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Claims 27-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Campos et al (US 6,911,206; see

entire document) in view of Lee et al (US 5,348,886; see entire document). **This is a new rejection.**

Applicants claim a method of cloning a gene comprising the steps of providing a naked circular replication-deficient baculovirus vector and a "rescue" vector encoding a nucleic acid that restores replication and a transgene. Functional genes are lacking in the baculovirus vector such as *lef*-2. The vector is furthermore capable of being maintained in bacteria.

Campos et al teach a method for cloning a fusion gene encoding a BHV-1 antigen and lutenizing hormone (gD:LH). The method involves providing a naked replication-deficient baculovirus vector and providing a transfer vector that comprises genes that complement for replication deficiency, or a rescue vector (see col 33, line 35- col 34, line 36). Campos et al do not teach any processes of linearization or digestion of the vector and therefore, absent evidence to the contrary, the vector is circular. The vectors are co-transfected into Sf21 insect cells as recited in part in claims 27 and 28.

Campos et al do not teach the use of a replication deficient baculovirus vector that is capable of being maintained in yeast or bacteria cells. Campos et al do not teach the specific gene that is deficient to render the baculovirus replication deficient.

Lee et al teach that baculovirus can be maintained in bacterial cells by insertion of a bacterial replicon and a selectable drug-resistance marker. This vector has the expected benefit that it can replicate in *E. coli* as a plasmid and is stably inherited and structurally stable after many generations of growth (see e.g. abstract).

Merrington et al teach that *lef-2* is a gene that encodes a gene necessary for viral replication (see e.g. page 338, col 2, paragraph 2). Merrington et al teach that the lef-2 mutation can be "rescued" by co-transfection of unmodified *lef-2*.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the replication defective baculovirus vector taught by Campos et al with the bacterial replicon and selectable marker as taught by Lee et al and by inactivation of the lef-2 gene as taught by Merrington et al because Campos et al teach that it is within the ordinary skill of the art to express replication defective baculovirus in a cell and because Lee teach that it is within the ordinary skill of the art to use bacteria as host cells for recombinant baculovirus vectors and because Merrington teaches that mutation of lef-2 affects DNA replication. One would have been motivated to do so in order to receive the expected benefit of expected benefit that it can replicate in *E. coli* as a plasmid and is stably inherited and structurally stable after many generations of growth (see abstract, Lee et al) and the expected benefit that Merrington et al have defined a gene involved in DAN replication and have demonstrated that a mutation in this gene can be rescued. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B. Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David Nguyen, PhD can be reached on (571)-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1633

~~Aril 15, 2005~~
1/9/2006

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER